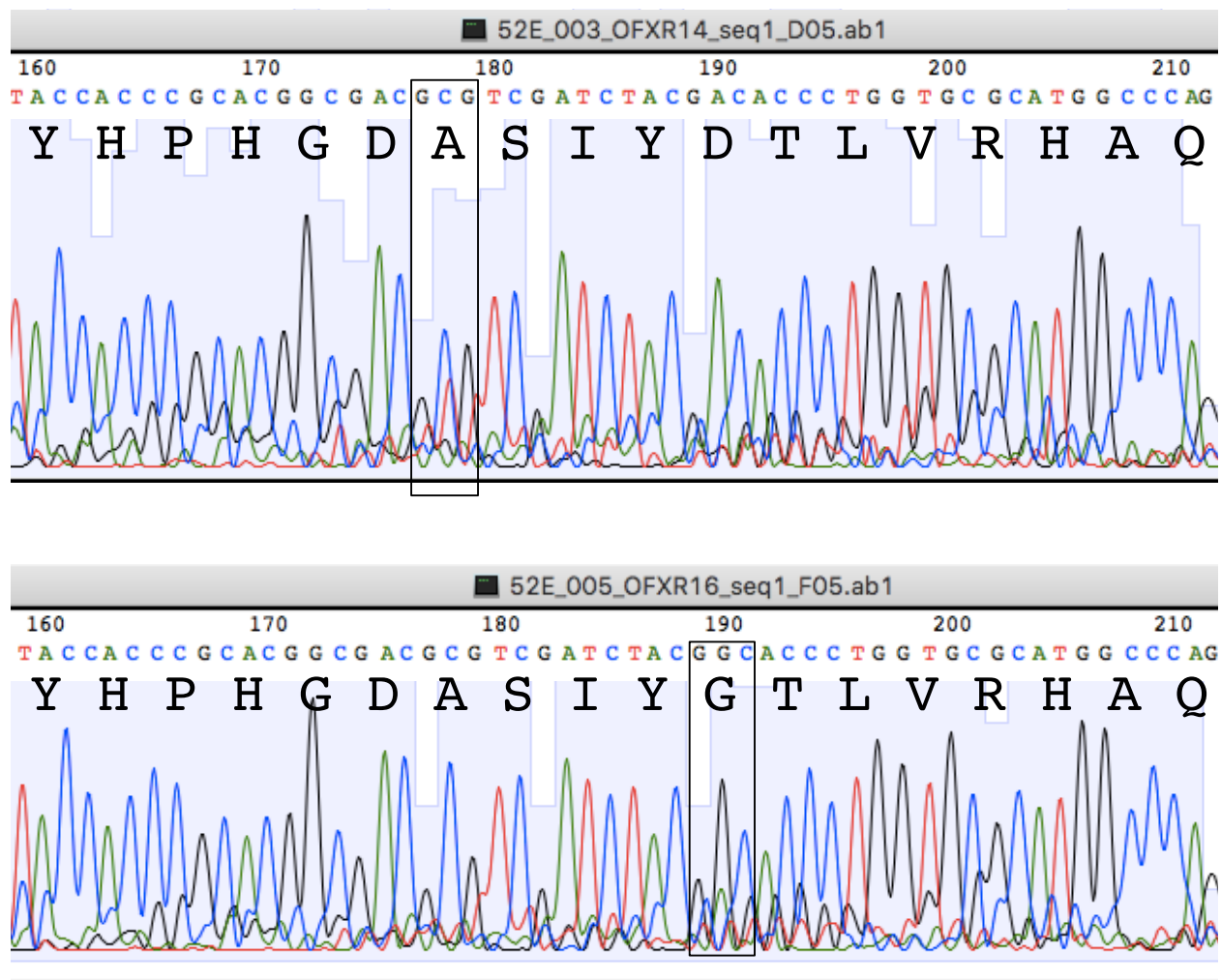


**Genomic analysis of the evolution of fluoroquinolone resistance in  
*Mycobacterium tuberculosis* prior to tuberculosis diagnosis**

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**Supplemental Materials**

- **SUPPLEMENTAL FIGURE 1. Sanger traces of *gyrA* PCR product from ambiguous samples**
- **SUPPLEMENTAL TABLE 1. SNP differences between clones isolated from original samples**



**Supplemental Figure 1. Sanger traces of *gyrA* PCR product from ambiguous samples.** Shown are the quinolone resistance determining regions from samples 14 and 16. In sample 14 (top), the alanine 90 codon GCG shows a clear minor T peak at the second position, while in sample 2, a minor A peak is seen in the second position of the glycine 94 codon (aspartic acid, codon GAC, is wt).

**SUPPLEMENTAL TABLE 1. SNP differences between clones isolated from original samples**

**Patient 1  
OFXR-2**

<b>position<sup>1</sup></b>	<b>clone</b>	<b>class<sup>2</sup></b>	<b>gene<sup>3</sup></b>	<b>protein<sup>4</sup></b>	<b>codon</b>	<b>AA<sup>5</sup></b>
7570	2R	NS	Rv0006	GyrA	GCG>GTG	A90V
1432840	2S	NS	Rv1280c	OppA	GCG>ACG	A201T
2468380	2R	S	Rv2203	CHP	GAC>GAT	
2875787	2S	S	Rv2555c	AlaS	GGC>GGG	
3252530	2S	NS	Rv2932	PpsB	ACG-GCG	T487A

**Patient 2  
OFXR-11**

<b>position<sup>1</sup></b>	<b>clone</b>	<b>class<sup>2</sup></b>	<b>gene<sup>3</sup></b>	<b>protein<sup>4</sup></b>	<b>codon</b>	<b>AA<sup>5</sup></b>
7572	11R3	NS	Rv0006	GyrA	TCG>CCG	S91P
7581	11R1	NS	Rv0006	GyrA	GAC>AAC	D94N
7582	11R2	NS	Rv0006	GyrA	GAC>GGC	D94G
800170	11S	IG	<Rv0699 Rv0700>			

**Patient 3  
OFXR-14**

<b>position<sup>1</sup></b>	<b>clone</b>	<b>class<sup>2</sup></b>	<b>gene<sup>3</sup></b>	<b>protein<sup>4</sup></b>	<b>codon</b>	<b>AA<sup>5</sup></b>
6579	14R2	NS	Rv0005	GyrB	TCC>TTC	S486F
7570	14R1	NS	Rv0006	GyrA	GCG>GTG	A90V
13061	14S	IG	Rv0009> <Rv0010c			
197785	14R1	NS	Rv0168	YrbE1B	ATC>ACC	I43T
284374	14R2	S	Rv0236c	AftD	ACC>ACT	
347536	14R2	S	Rv0284	EccC3	ACA>ACC	
396125	14S	IG	<Rv0330c Rv0331>			
580548	14S	S	Rv0490	SenX3	AAC>AAT	
756614	14R1	NS	Rv0663	AtsD	GGG>AGG	G160R
1017055	14R1	IG	Rv0912 > <Rv0913c			
1598662	14R1	NS	Rv1423	WhiA	GAT>TAT	D253Y
1741178	14R1	S	Rv1537	DinX	ATC>ATT	
2058051	14R2	NS	Rv1815	CHP	CCG>CTG	P175L
2120894	14R2	S	Rv1870c	CHP	GCG>GCA	
2301782	14R2	S	Rv2048c	Pks12	GTA>GTG	
2301782	14R1	S	Rv2048c	Pks12	GTA>GTG	
2308552	14R1	NS	Rv2051c	Ppm1	ACG>AAG	T735K
2602958	14R1	S	Rv2329c	NarK1	AAC>AAT	
2853818	14R1	NS	Rv2529	hypot	GCC>GAC	A315D
2873918	14R2	NS	Rv2555c	AlaS	GAC>GAA	D856E
3140303	14S	NS	Rv2833c	UgpB	CAG>CGG	Q61R
3186286	14R2	NS	Rv2874	DipZ	AAA>AAC	K480N
3369036	14S	NS	Rv3010c	PfkA	CAC>CAG	H273Q
3403159	14R1	NS	Rv3042c	SerB2	CCA>TCA	P2S
3492131	14S	IG	<Rv3126c Rv3127>			
3665331	14R1	NS	Rv3283	SseA	GAA>GGA	E135G
3842787	14S	IG	Rv3425> Rv3426>			
4081276	14R1	S	Rv3643	hypot	GCC>GCG	

**Patient 4**  
**OFXR-15**  
**OFXR-16**

<b>position</b> <sup>1</sup>	<b>clone</b>	<b>class</b> <sup>2</sup>	<b>gene</b> <sup>3</sup>	<b>protein</b> <sup>4</sup>	<b>codon</b>	<b>AA</b> <sup>5</sup>
7566	16R2	NS	Rv0006	GyrA	GAC>AAC	D89N
7570	16R3	NS	Rv0006	GyrA	GCG-GTG	A90V
7582	15R	NS	Rv0006	GyrA	GAC>GGC	D94G
7582	16R1	NS	Rv0006	GyrA	GAC>GGC	D94G
399110	16R1	S	Rv0334	RmlA	GGC>GGT	
686405	16S	S	Rv0588	YrbE2B	CTG>TTG	
1439105	15R	NS	Rv1286	CysN/C	GGC>GAC	G67D
1439105	16R1	NS	Rv1286	CysN/C	GGC>GAC	G67D
1439105	16R3	NS	Rv1286	CysN/C	GGC>GAC	G67D

\*Excluding SNP calls in repetitive regions

<sup>1</sup> Genome coordinates and wild-type sequence based on H37Rv reference NC\_000962.3

<sup>2</sup> IG = intergenic, S = synonymous, NS = non-synonymous

<sup>3</sup> Intergenic SNPs are represented by flanking genes, with arrows indicating direction of transcription

<sup>4</sup> CHP= conserved hypothetical protein, hypot = hypothetical protein

<sup>5</sup> Resulting change in protein; blank if no change